

Application No.: 10/031,241  
Inventor: HAUER et al.  
Reply to Office Action of 25 January 2006  
Docket No.: 50531

### REMARKS/ARGUMENTS

Claims 1-22 are currently pending. Claims 11-12 and 16 are amended.

#### **Claim Objections**

The Examiner has objected to claim 11 for being dependent from a non-elected claim. The Examiner also objects to claim 16 because "zinc" is spelled incorrectly. In light of the amendments to claims 11 and 16, Applicants respectfully request withdrawal of the instant objections. Favorable action is solicited.

#### **Claim Rejections Under 35 USC §112 ¶2**

Claims 11-12 and claims 16-18 are rejected for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention.

Applicants' amendments deleting the term "hydroxylatable" render the instant rejection moot. Withdrawal of the instant rejection is respectfully requested and favorable action is solicited.

#### **Claim Rejections Under 35 USC §112 ¶1**

Claims 11-12 and 16-18 are rejected for allegedly failing the written description prong of §112. Applicants respectfully disagree.

In regards to all the 112 ¶1 rejection, it must be remembered that to satisfy the written description prong of 35 USC §112 ¶1, the specification must only describe the invention in sufficient detail so that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997). No particular form of disclosure is required, but "the description must clearly allow persons of ordinary skill in the art to recognize that [the patentee] invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989) (citing *In re Wertheim*, 541 F.2d 257, 262 (CCPA 1976)).

Applicants respectfully assert that the Examiner's use of the stand USPTO biotechnology

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rejection is misplaced. The instant rejection is for an isolated gene and/or gene product. In contrast, the instant claims are directed to a novel method for the enzymatic production of terminally or subterminally hydroxylated fatty acids. Thus, Applicants respectfully submit that the rejection is not directed to the Applicants claims.

Additionally, the MPEP states that a "[d]escription of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces" and as such, a single species may be enough to identify the entire genus (*see* MPEP 2163.II.A.3.a.ii.). A recent Federal Circuit case supports the statements of the MPEP. When discussing what is required for a written description the court said "[t]he 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution" (*Capon v. Eshhar*, 418 F.3d 1349, 1358; 2005). Further, in overturning a BPAI decision, which relied on similar rejection reasons as stated in the instant Office Action, where both parties to an interference had all claims in their respective patents cancelled for failing to meet the written description requirement, the court stated that "[t]he Board erred in refusing to consider the state of the art of the scientific knowledge" and when citing *Lilly* and *Fiers* spoke of a rulings in view of a "wish" list provided in said inventions, and not the state of the relevant art (*Id.* at 1357). Further still, the court stated, that "[i]t is not necessary that every permutation with a generally operable invention be effective in order for an inventor to obtain a generic claim" and both parties were lauded because they "present[ed] not only general teachings... but also specific examples" (*Id.* at 1359).

Applicants respectfully assert that the instant specification fully complies with all the aforementioned requirements because it allows one of ordinary skill in the art to practice the instant invention. Applicants provide in the instant specification summary information such as the function of electron donor transfer systems and general biological techniques which meet the "general teachings" prong. Further, Applicants have supplied "specific examples" of the instant invention as required of the second prong of *Capon*. The instant specification teaches at least the

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specific zinc/Co(III) sepulchrane electron donor system.

Moreover, cytochrome P450 monooxygenase is one of the most widely studied enzymes. For example, a search of the National Center for Biotechnology Information<sup>1</sup> provided 45,000+ articles for the search term "cytochrome P450 monooxygenase" up to the filing date of the instant application. Thus, the combination of the teachings, suggestions and disclosure of the instant invention with the knowledge of one of ordinary skill in the art would provide all the requirements for the 112 written description requirement.

In view of at least the above, Applicants respectfully request withdrawal of the instant written description rejection and favorable action is requested.

Regarding the enablement requirement of §112, the Federal Circuit has held that "[t]he specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation'." (*Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1334 (Fed. Cir. (2003))). The claims, as currently amended, are fully enabled by the specification of the instant application in combination with the general knowledge of one of ordinary skill in the art. One of ordinary skill in the art would clearly be able to practice the instant invention in light of the instant amendments.

Further, it is not necessary that the application describe the presently-claimed invention exactly, but only sufficiently clearly that one of ordinary skill in the art would recognize from the disclosure that the appellants invented it. (See, *In re Edwards*, 568 F.2d 1349, 1351-52 (CCPA 1979); *In re Wertheim*, 541 F.2d 257, 262 (CCPA 1976)) "[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims." *Wertheim* at 263. Applicants respectfully submit that the Examiner has not presented evidence or reasons why the instant invention is not enabled. The inventors of the instant application, via their signed oath concurrent with the filing of said application, assert that the invention is enabled. The Examiner

<sup>1</sup> <http://www.ncbi.nlm.nih.gov/>

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has not shown otherwise or provided any evidence to the contrary.

Further still, as described in *Capon*, as the skill in the art progresses so does the analysis of the inventions in said art. The Examiner alleges that the instant disclosure does not enable a method for hydroxylating any and all fatty acids. Applying *Capon* and the relative state of the art at the time of filing, one of ordinary skill would be able to create any and all of the fatty acids the Examiner asserts would require undue experimentation. First, the guidance needed would be minimal, if any was needed at all, as hydroxylating techniques are well known to the skilled artisan. The skill in the art at the time of filing was such that creation of fatty acids, in general, was routine. Second, The Examiner asserts that undue experimentation would be required to practice the invention as claimed. However, *In re Wands* states: "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed" (*In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988))(quoting *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (Bd. App. 1982)) (applying this principle in the context of monoclonal antibody production). Any experimentation associated with the instant invention would be routine to one of ordinary skill in the art.

Additionally, the Examiner has erroneously mandated a quantifiable number of examples from the Applicants in order for the instant invention to be enabled. As the Examiner is well aware, Applicants are not required to provide even a single working example (*See, In re Gosteli* above - no specific form of the disclosure is required). Thus, any requirement for a mandatory number of examples is contrary to USPTO practice and as such, the Examiner's statement indicating an insufficiency in the number of examples disclosed in the instant specification is in error. If, contrary to Applicants assertions that the instant invention is enabled, the Examiner has used information from examples not of record, Applicants respectfully request an Examiner's affidavit indicating the use of personal knowledge and allowance for Applicants to respond to said personal knowledge.

Furthermore, the term "cytochrome P450 monooxygenase" is used generically because that is how one of ordinary skill in the art would understand the term. Contrary to the

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Examiner's assertions, one of ordinary skill in the art would consider any cytochrome P450 monooxygenase to be enabled in the instant invention. Applicants respectfully assert that there is nothing on the record to indicate otherwise. Again, if the Examiner has personal knowledge regarding the efficacy of cytochrome P450 monooxygenase, Applicants respectfully request submission of an Examiner's affidavit and the opportunity to respond.

For at least the aforementioned, the instant claims, as currently amended, are fully enabled by the specification of the instant application in combination with the general knowledge of one of ordinary skill in the art. Accordingly, Applicants respectfully request withdrawal of the instant enablement rejection and favorable action is solicited.

#### **Claim Rejections Under 35 USC §102**

Claims 11-12 and 17-18 stand rejected as allegedly anticipated by Estabrook et al. Applicants respectfully disagree.

Anticipation can only be established by a single prior art reference which discloses each and every element of the claimed invention. *RCA Corp. v. Applied Digital Data Systems, Inc.*, 730 F.2d 1440, 1444, 221 USPQ 385, 388 (Fed. Cir. 1984). The identical invention must be shown in as complete detail as it is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). It is not enough, however, that the reference discloses all the claimed elements in isolation. Rather, as stated by the Federal Circuit, the cited art reference must disclose each element of the claimed invention "arranged as in the claim." *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983).

Estabrook et al fails to teach, suggest or disclose that the source of electrons is a metal powder form with a lower standard normal potential than the mediator of amended claim 11 and as such, fails to anticipate claim 11 and all claims dependent therefrom.

Accordingly, since Estabrook et al. does not teach, suggest or disclose each and every element as arranged of claim 11, it does not anticipate claim 11. Applicants therefore respectfully request withdrawal of the rejection under 35 USC § 102(b). Favorable action is solicited.

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### Claim Rejections Under 35 USC §103

Claim 16 stands rejected as allegedly unpatentable over Estabrook et al. in view of Creaser et al. Applicants respectfully disagree

To establish *prima facie* obviousness, the Examiner must show in the prior art some suggestion or motivation to make the claimed invention, a reasonable expectation for success in doing so, and a teaching or suggestion of each claim element (*See, e.g., In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ 2d 1941 (Fed. Cir. 1992); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)). Most inventions arise from a combination of old elements and each element may often be found in the prior art (*In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998)). However, mere identification in the prior art of each element is insufficient to defeat the patentability of the combined subject matter as a whole (*Id.* at 1355, 1357). Rather, to establish a *prima facie* case of obviousness based on a combination of elements disclosed in the prior art, the Examiner must articulate the basis on which it concludes that it would have been obvious to make the claimed invention (*Id.*). In practice, this requires that the Examiner "explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious" (*Id.* at 1357-59). This entails consideration of both the "scope and content of the prior art" and "level of ordinary skill in the pertinent art" aspects of the *Graham* test.

Known compositions do not render an invention obvious simply because they could be combined; to establish a *prima facie* case of obviousness, the Examiner must provide a rationale for said combination. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination<sup>2</sup>. Moreover, the question regarding whether to combine references must be complete. It must be based on objective evidence of record. This precedent has been reinforced

<sup>2</sup> See, *In re Mills*, 916 F.2d 680 (Fed. Cir. 1990).

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in myriad decisions, and cannot be disregarded<sup>3</sup>. Applicants assert that there is no motivation to combine the cited art references the Examiner has used as a basis for the §103 rejection. Applicants emphasize that one of ordinary skill at the time of filing of the instant application would not be motivated to combine the art cited by the Examiner.

Applicants also note that even though the reduction of the Co(III) complex with zinc dust, as disclosed by Creaser et al, was described for the first time almost 25 years before the priority date of the present invention and almost 20 years before the work of Estabrook was published, neither Estabrook et al. nor Faulkner et al. nor any other group working in the instant technical field has mentioned the work of Creaser (or the corresponding US patent of Sargeson, US 4,497,737). More specifically, the Examiner is directed to the work of Fang (1996)(IDS as filed) wherein said art references the work of Faulkner et al. (See page 1282, left column, 2nd paragraph). Starting from the electrode-based electron donor system of Faulkner et al., Fang suggests employing dithionite as a reducing agent for the P450 enzyme. Thus, one of ordinary in the art, starting from the electrode-based electron donor system of Estabrook et al., would have expected success with a reducing agent which is soluble in the reaction mixture, as for example dithionite, rather than the metal-based system of Creaser et al./Sargeson et al. which, according to Sargeson (See column 4, lines 60-65) was regarded as a suitable redox system for inorganic and organic synthesis rather than biosynthesis.

Accordingly, one of ordinary skill in the art would not have been motivated to combine the art cited by the Examiner with the expectation for success in practicing the instant invention.

Further, Applicants reassert that the Examiner has engaged in impermissible hindsight reasoning. There must be a reason apparent at the time the invention was made to a person of

<sup>3</sup> See, e.g., *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1124-25 (Fed. Cir. 2000) ("a showing of a suggestion, teaching, or motivation to combine the prior art references is an 'essential component of an obviousness holding'") (quoting *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1352 (Fed. Cir. 1998)); *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."); *In re Dance*, 160 F.3d 1339, 1343 (Fed. Cir. 1998) ("there must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant"); *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988) ("teachings of references can be combined only if there is some suggestion or incentive to do so.") (emphasis in original) (quoting *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577 (Fed. Cir. 1984)).

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ordinary skill in the art for applying the teaching at hand, or the use of teaching as evidence of obviousness will entail prohibited hindsight (*In re Nomiya, Kohisa, and Matsumura*, 509 F.2d 566 (CCPA 1975)). While it is correct that Creaser et al. discloses a reaction between cobalt sepulchrate and Zn dust, said reference fails to teach, suggest or disclose that the system might also be applied, under physiological conditions, in enzyme-catalyzed hydroxylation reactions of fatty acids of the claimed type. The suggested treatment of said complex with zinc dust and HCl (*See*, US 4,497,737, column 4, lines 20-23) does not represent physiological conditions applicable to enzyme-catalyzed reactions.

Further still, Applicants again refer the Examiner to the data from the experimental work of the inventors submitted in the reply of 12 February 2004 (attached hereto for the convenience). Similar to the experiments performed by Estabrook et al., and summarized in Table I of said reference, the instant inventors compared reaction rates for the BM-3 mutant F87A under conditions similar to the cited art and also to the claimed invention. Artificial substrate 12-pNCA was used as the enzyme substrate to measure activity via an optical test. Enzyme activity was measured in separate reactions in either the presence of NADPH or electrolysis/Pt-electrode (Estabrook et al.) and NADPH or Zn dust and Co(III) sepulchrate (instant invention) as electron sources. With the NADPH reactions set to 100%, the inventors of the instant claimed invention surprisingly demonstrate that Zn dust and Co(III) sepulchrate reaction had a relative reaction almost twice as great as that of the Estabrook et al. example. These data show that the electron donor system of the instant invention is more suitable for enzyme reactions of the claimed type because of the higher reaction rates.

In view of at least the above, Applicants believe the Examiner has engaged in prohibited hindsight reasoning to arrive at the present invention. To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher. *W. L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). The only suggestion for the instant invention is from the instant invention.



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The Examiner believes that Applicants have attacked the references individually in regards to the above mentioned argument. Applicants respectfully disagree. The Examiner has attempted to piece together the claimed invention using the instant claims as a guide picking and choosing elements to fit an obviousness rejection. As the court stated in *In re Fritch*, "[i]t is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teaching of the prior art so that the claimed invention is rendered obvious" (972 F.2d 1260, Fed. Cir. 1992). Applicants have merely pointed out where and why in the cited art they believe the Examiner has impermissible used hindsight reasoning to piece together said cited art.

Applicants have looked at the references as a whole, as required by the MPEP and the Federal Circuit, and pointed out where and why the references fail to teach, suggest or disclose the instant invention, alone or in combination. This is not attacking the references individually and the Examiner is reminded of following from MPEP 2142

If the examiner determines there is factual support for rejecting the claimed invention under 35 U.S.C. 103, the examiner must then consider any evidence supporting the patentability of the claimed invention, such as any evidence in the specification or any other evidence submitted by the applicant. The ultimate determination of patentability is based on the entire record, by a preponderance of evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence. *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). (emphasis added)

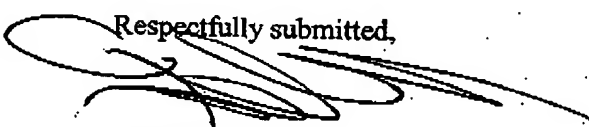
For at least the reasons expressed above, it is urged that the art references cited by the Examiner, either singly or in combination, fail to teach, suggest or disclose the instant invention as defined by the claims. Accordingly, a *prima facie* case of obviousness has not been established by the Examiner, and the rejection under 35 USC §103 should be withdrawn. Favorable action is solicited.

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Conclusion

Applicants respectfully submit that the present application is in condition for allowance, which action is courteously requested. Please charge the two-month extension fee to the credit card listed on the enclosed Form PTO-2038. Please charge any shortage in fees due in connection with the filing of this paper to Deposit Account 14.1437. Please credit any excess fees to such account.

Respectfully submitted,



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